Brain SPECT when structural imaging fails to offer diagnostic clues.

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Structural imaging modalities such as CT and especially MRI offer the opportunity to visualize brain anatomy in great detail. CT is widely used now in veterinary medicine and the imaging modality of choice in most centres. Indeed in many cases CT offers an answer to neurological questions. However, when available, MRI is superior for imaging pathologies other than acute brain haemorrhage. The images are excellent and by using the different sequences, composition of tissue can be determined and differentiated which improves the diagnostic potential.
The higher the strength of the magnet, the better anatomical detail will be. With a 7-Tesla magnet, resolution of 0,1 mm can be obtained which reaches the histological resolution level. With this magnet even small vessel defects in cerebrovascular disease are visualized.
However, these imaging modalities are great to demonstrate structural pathology, but fail when pathology is strictly functional without anatomical alterations.
Brain Single Photon Emission Tomography (SPECT) is a functional imaging modality based on the use of radioactive markers. After IV injection, these compounds will pass the blood brain barrier and will be trapped inside the neuron by enzymatic conversion. This mechanism implies two conditions, first the amount of tracer reaching the different brain regions will depend on the regional perfusion. Already in the 19th century, it was demonstrated in dogs that regional brain blood flow correlates with neuronal function. Decreased function is translated in reduced blood flow. Second, the neuron has to function normally in order to enable enzymatic conversion of the tracer. Two tracers can be used for this purpose, ^{99m}Tc-HMPAO and ^{99m}Tc-ECD, each with basically similar trapping mechanisms. These markers will thus reflect regional blood flow (hypo- or hyperperfusion) and associated neuronal function(hypo- or hyperfunction). An advantage is that, due to the trapping mechanism, imaging after injection of the tracer, can be postponed for a certain time. The images obtained after that time interval, will reflect the functional state of the brain at the time of injection. This is an interesting characteristic, especially of use in epileptic patients during an epileptic fit, the optimal time to localize the focus of activity, but also an impossible time to obtain images. In people with refractory epilepsy SPECT is used presurgically to detect the seizure focus. Images are obtained interictally and at the onset of the fit. The start of the injection can be coordinated with the onset of the seizure by means of EEG activity registration. However, often the patient will start the injection him/herself at the time he/she feels the seizure starting. After analysing the images by visual inspection or even better by subtraction analysis (Ictal data-interictal data) the focus will be determined which will be surgically removed if possible. In this lecture, some preliminary canine results will be demonstrated. Dogs with primary epilepsy were investigated with SPECT in the interictal state. A reduced activity was

registered in the subcortical area. Due to resolution limits at the time of that investigation, we were not able to define the subcortical structures more into detail. However, this subcortical region includes the thalamus, a region often allocated as being involved in seizure progression. Recently, new software and Hi-SPECT became available for the use in dogs. These techniques improve the resolution to a great extent. This paves the way to explore the subcortical areas in more detail.

Also in behaviour disorders brain SPECT may be advantageous. Unless structural pathology provokes behaviour disturbances, CT and MRI are useless in the investigation of behaviour disordered animals. Since brain perfusion reflects neuronal function, dysfunctioning brain regions can be recognised. The two most important brain structures responsible for behaviour are the frontal cortex and the limbic system. These two have to work in complete harmony with each other; the frontal cortex reflecting the actions impelled by the limbic system on sensorial triggers from the outside. If in disharmony, inappropriate reactions will evolve, triggered by stimulation from the outside. In many behaviour disorders alterations are present in these areas. However, this is an oversimplification and other brain regions may be involved, as the brain is one large electrical circuit with many relays. In addition to good functioning neurons, neurotransmitter systems have to function in an optimal way as well to secure normal behaviour. The probably best known neurotransmitter systems are the serotonergic, dopaminergic and noradrenergic system. However, the list is of course longer. The serotonergic system is considered as one of the most important systems in maintaining normal behaviour. I am convinced that everyone is familiar with the compound “Prozac”, used as a mood stabilizer, with its major action on the serotonergic system by increasing the amount of serotonine available in the brain. As an example, impulse control disorders are linked with deficiencies in the serotonergic system. Several studies including a variety of animals (from primates to spiders) demonstrated that a low serotonergic tone in the brain is linked with “risk taking” or “impulsive” behaviour. Another important pathway in behaviour is the dopaminergic system, involved in Parkinson’ disease amongst other disorders.

For several compounds (receptors, transporters..) of these neurotransmitter systems, specific radioactive tracers have been developed. These markers will specifically bind with their target and will give an idea of the number of receptors and transporters present in different brain regions. In the diseased brain deficiencies of neurotransmitter systems can be detected in this way. We investigated dogs with several specific behaviour abnormalities: impulsive aggression, anxiety disorders and compulsive disorders. Depending on the disorder, abnormalities were present at the level of the serotonergic receptor 2A, the serotonergic transporter and the dopaminergic transporter in specific brain areas. Another important domain for investigation, is in vivo registration of effects of (psycho)pharmaca. With these specific markers a prediction can be made whether or not certain psychopharmaca will be useful in a particular patient and therapy outcome can be monitored. Effect on neuronal activity and interaction with neurotransmitter systems can be investigated, optimal dosing can be explored. This imaging modality is, besides its use in a clinical set-up, also an important asset in research and development of new compounds.

In conclusion, SPECT imaging with dedicated tracers is an important additive tool to CT and MRI in the investigation of epilepsy, behavioural problems and effect of drugs on neurons and transmitter systems.

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